IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.:	4,182,763
Named Inventors:	George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr.
For:	BUSPIRONE ANTI-ANXIETY METHOD
Issued:	January 8, 1980
Serial No.:	908,597
Filed:	May 22, 1978
Group Art Unit:	125
Examiner:	Stanley J. Friedman

#9 petition R 3/24

RECEIVED NOV 22 1985 DEPUTY ASST. COMM.

RECEIVED OCT 4 1985 GROUP 120

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

PETITION UNDER 37 C.F.R. §1.324 FOR CORRECTION OF INVENTORSHIP IN PATENT

Sir:

The named inventors on U.S. Patent No. 4,182,763, George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr.; an inventor that was not named through error, John E. Gajewski; and, the assignee of record, Mead Johnson & Company, hereby petition the Honorable Commissioner of Patents and Trademarks to issue a certificate naming the actual inventors on said patent.

This Petition is supported by:

(a) Verified Statements of Fact and Declarations of George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. Under 37 C.F.R. §1.324.

(b) Verified Statement of Fact and Declaration of John E. Gajewski Under 37 C.F.R. §1.324.

(c) Verified Statement of Fact and Declaration of Robert E. Carnahan Under 37 C.F.R. §1.324.

(d) Declaration, Power of Attorney and Petition Under 37 C.F.R. §1.63 For Application S.N. 908,597 Now U.S. Patent No. 4,182,763.

(e) Consent of Assignee.

(f) Proposed Certificate of Correction.

Please charge the Petition fee of $120.00 [37 C.F.R. §1.20(b)] to Deposit Account No. 02-3825.

The Commissioner of Patents and Trademarks is hereby authorized to charge Deposit Account No. 02-3825 with any additional fees which may be required in connection with this Petition, including, but not limited to a title search report in connection herewith.

It is respectfully submitted that the attached Verified Statements establish that John E. Gajewski is an inventor, and was not named on the patent through error without deceptive intention on the part of the actual inventors.

Respectfully submitted,

Dated: October 2, 1985

Robert E. Carnahan

Robert E. Carnahan
Reg. No. 18,500
Agent for the Named Inventors,
John E. Gajewski, and Mead
Johnson & Company
Bristol Laboratories
Bristol-Myers Company
P.O. Box 4755
Syracuse, New York 13221-4755
(315) 432-4813

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Patent No.:	4,182,763
Named Inventors:	George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr.
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Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

VERIFIED STATEMENTS OF FACT AND DECLARATIONS OF GEORGE P. CASTEN, GORDON R. McKINNEY, ROGER E. NEWTON, E. CROSBY TOMPKINS AND JOHN H. WEIKEL, JR. UNDER 37 C.F.R. §1.324

GEORGE P. CASTEN, GORDON R. McKINNEY, ROGER E. NEWTON, E. CROSBY TOMPKINS AND JOHN H. WEIKEL, JR. (hereinafter referred to jointly as the "named inventors") state and declare, individually as indicated and jointly as indicated:

1. I, GEORGE P. CASTEN, am the named GEORGE P. CASTEN, one of the named inventors on U.S. Patent No. 4,182,763 that was issued on January 8, 1980 and is entitled "Buspirone Anti-Anxiety Method." I am currently employed by the Pharmaceutical Research and Development Division of the Bristol-Myers Company at its facilities in Evansville, Indiana in the capacity of Senior Research Scientist and have been so employed in this capacity since 1982. At all prior relevant times herein I was employed in a similar capacity by the Mead Johnson & Company subsidiary of the Bristol-Myers Company in

Evansville, and specifically between 1971 and 1978 I was involved in the regulatory affairs of Mead Johnson and between 1978 and 1982 I became a Senior Research Scientist of Mead Johnson. I currently reside at 7416 Adams Avenue, Evansville, Indiana 47715.

2. I, GORDON R. McKINNEY, am the named GORDON R. McKINNEY, one of the named inventors on U.S. Patent No. 4,182,763 that was issued on January 8, 1980 and is entitled "Buspirone Anti-Anxiety Method." I am currently employed by the Mead Johnson & Company subsidiary of the Bristol-Myers Company at its facilities in Evansville, Indiana in the capacity of Director of Medical Communications and have been employed in this capacity since 1980. Prior to 1980 and at all relevant times herein I was employed by Mead Johnson in Evansville, ~~to perform the same function, and~~ specifically between 1968 and 1975 I was the Director of Pharmacology, between 1975 and 1978 I was the Director of Biological Research, and between 1978 and 1980 I was the Associate Director of Medical Services. I currently reside at 421 Kings Valley Road, Evansville, Indiana 47711.

3. I, ROGER E. NEWTON, am the named ROGER E. NEWTON, one of the named inventors on U.S. Patent No. 4,182,763 that was issued on January 8, 1980 and is entitled "Buspirone Anti-Anxiety Method." I am currently a consultant to the Pharmaceutical Research and Development Division of the Bristol-Myers Company. During the period between May 1966 and 1982 I was employed by the Mead Johnson & Company subsidiary of the Bristol-Myers Company in Evansville, Indiana, and between 1982 and 1984 I was employed by the Pharmaceutical

Research and Development Division of the Bristol-Myers Company in Evansville in the capacity of Associate Medical Director and Director of Clinical Research. I currently reside at 1400 Lark Drive, Evansville, Indiana 47715.

4. I, E. CROSBY TOMPKINS, am the named E. CROSBY TOMPKINS, one of the named inventors on U.S. Patent No. 4,182,763 that was issued on January 8, 1980 and is entitled "Buspirone Anti-Anxiety Method." I am currently employed by Toxicity Research Laboratories in its facilities in Muskegon, Michigan in the capacity of Vice President and Director of Toxicology since 1978. I was employed by the Mead Johnson & Company subsidiary of the Bristol-Myers Company in 1970 as a Senior Investigator and in 1978 I became a Principal Investigator. I was employed at the Mead Johnson facilities in Evansville, Indiana. In 1978 I left the employ of Mead Johnson and became employed by Toxicity Research Laboratories. I currently reside at 15119 Fairmont Court, Grand Haven, Michigan 49417.

5. I, JOHN H. WEIKEL, JR., am the named JOHN H. WEIKEL, JR., one of the named inventors on U.S. Patent No. 4,182,763 that was issued on January 8, 1980 and is entitled "Buspirone Anti-Anxiety Method." I am currently employed by the Pharmaceutical Research and Development Division of the Bristol-Myers Company at its facilities in Evansville, Indiana in the capacity of Director of Pathology and Toxicology and have been so employed at all relevant times herein. Prior to 1982 I was employed in a similar capacity by the Mead Johnson & Company subsidiary of the Bristol-Myers Company in

Evansville. I currently reside at R.R. #4, Box 266, Mount Vernon, Indiana 47620.

6. The named inventors make this statement and declaration in support of the petition to the Commissioner of Patents and Trademarks to correct the inventorship of U.S. Patent No. 4,182,763 by adding the name of John E. Gajewski as an inventor on the '763 patent.

7. At the time that the named inventors signed the declaration for said S.N. 908,597, they believed, individually and jointly, that they, and only they, jointly made the invention disclosed and claimed in said S.N. 908,597. The invention, as defined in the claims is for:

> "A method for the palliative treatment of neurosis in which anxiety symptoms are prominent which comprises administering a non-toxic anxiolytically effective dose of buspirone or a pharmaceutically acceptable acid addition salt thereof to a neurotic patient." (Claim 1.)

The dependent claims define, inter alia, route of administration and daily dose quantities.

8. The named inventors continued to believe that they were the only joint inventors of the invention of the '763 patent until the time that they were shown a document that was prepared by Dr. John E. Gajewski. [Attached hereto as Exhibit A.] The document was dated April 23, 1974, which was prior to the time that the named inventors made the invention beginning in about mid-1975.

9. Each named inventor individually states with respect to himself:

(a) That he saw Exhibit A for the first time between about late 1984 and about September 1985;

(b) That he did not know of the existence of Exhibit A prior to the first time that he saw it;

(c) That he did not know that Dr. Gajewski had prepared Exhibit A prior to the first time that he saw it;

(d) That he was shown Exhibit A for the first time by patent attorneys for the assignee of the '763 patent;

(e) That he was advised by said attorneys of the meaning within the context of the U.S. patent laws of "inventorship," and he was advised of the requirement for naming all inventors on a U.S. patent application and patent; and

(f) That he, after reading and understanding Exhibit A, and accepting the advice of said attorneys, now believes that Dr. Gajewski is a joint inventor of the invention disclosed and claimed in the '763 patent.

10. The named inventors, individually and jointly, now realize and believe that an error was made in failing to include Dr. Gajewski as an applicant and joint inventor on S.N. 908,597 and as a joint inventor on the '763 patent, together with the named inventors.

11. The named inventors, individually and jointly, believe that the error in not including Dr. Gajewski on S.N. 908,597 occurred because of their lack of knowledge of the existence of Exhibit A. The named inventors believe that the reason that none of them saw or knew about Exhibit A prior to the time it was shown to each of them, as set forth in Paragraph 9, above, is that none of them were in the chain of

responsibility at Mead Johnson and Bristol-Myers that would have been the basis for any of them receiving a copy of Exhibit A and/or being advised of its existence.

12. The named inventors, individually and jointly, understand that Exhibit A describes the method of at least claim 1 of the '763 patent, particularly by suggesting the usefulness of buspirone as an antianxiety agent in neurotic patients.

13. The named inventors believe that the application that was filed as S.N. 908,597 was prepared by Dr. Robert E. Carnahan, a patent agent employed by the Bristol-Myers Company. To the best of their recollection, individually and jointly, Dr. Carnahan reviewed those internal documents of Mead Johnson that were dated contemporaneously with the making of the joint invention by the named inventors (i.e., about mid-1975), and later, and in discussions with the named inventors, they jointly and individually expressed to Dr. Carnahan their then held belief that the named inventors were the only joint inventors. They also believe, that at the time Dr. Carnahan prepared the application, Dr. Carnahan, based on such information as described above, believed that the named inventors were the only joint inventors, and he prepared and sent to the named inventors the declaration for the named inventors. The named inventors signed the declaration in the belief that they were the only joint inventors.

14. In view of the facts as set forth above, and the explanations made to the named inventors by said attorneys

with respect to the meaning of the term "inventorship," the named inventors, individually and jointly, believe that Dr. Gajewski is a joint inventor together with the named inventors for the subject matter described and claimed in the '763 patent, and that Dr. Gajewski was omitted as a joint inventor together with the named inventors through error. The named inventors believe, individually and jointly, that such error occurred without any deceptive intention by any of the named inventors, or Dr. Gajewksi, or anyone else involved with the preparation and prosecution of S.N. 908,597 or anyone else in privy with any of these people, and the named inventors have no reason to believe that the error occurred with deceptive intention.

15. The named inventors are informed and believe, individually and jointly:

(a) That the error without deceptive intention was discovered by one of the attorneys who first showed the named inventors Exhibit A;

(b) That the attorney had come across document Exhibit A during the course of his review of older Mead Johnson documents (i.e., dated prior to about mid-1975) bearing on busipirone as an antipsychotic agent in connection with his assigned task of reviewing the '763 patent, including the history of the making of the invention claimed in the '763 patent;

(c) That the review by the attorney was commenced in about late 1984 at which time he began to gather information in aid of his review of the '763 patent;

(d) That Exhibit A was discovered by the attorney in the course of gathering the information in about late 1984;

(e) That the attorney continued his investigation and review of the '763 patent for several more months prior to preparing his report in about April 1985;

(f) That the attorney together with other attorneys of Bristol-Myers thereafter undertook further legal and factual (including further interviews) analyses and considerations on the question of whether Dr. Gajewski was a joint inventor;

(g) That it was not until about August 1985 that the decision was made to petition the Commissioner of Patents and Trademarks for a Certificate of Correction to add the name of Dr. Gajewski as an inventor on the '763 patent; and

(h) That it took about two months to complete the necessary interviews and the necessary papers that were required to prepare the petition for the Certificate of Correction to correct the inventorship of the '763 patent.

16. In view of the facts as set forth above, the named inventors, individually and jointly, believe that it was in about mid-1985 that the error was discovered to exist in fact.

17. Accordingly, the named inventors petition the Commissioner of Patents and Trademarks to correct the inventorship error and issue a Certificate of Correction that adds the name of John E. Gajewski as an inventor on the '763 patent.

We, the named inventors hereby declare, individually and jointly, that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the '763 patent.

Dated: 9-26-85 George P. Casten

Dated: Sept. 27, 1985 Gordon R. McKinney

Dated: September 25, 1985 Roger E. Newton

Dated: September 30, 1985 E. Crosby Tompkins

Dated: September 26, 1985 John H. Weikel, Jr.

BRISTOL-MYERS COMPANY
PHARMACEUTICAL, HEALTH CARE, AND INTERNATIONAL GROUP
R & D PROJECT EVALUATION
I - NARRATIVE SUMMARY

PROJECT/~~PROGRAM~~ (6)	B-M DIVISION
Buspirone - Project 9022	Mead Johnson and Company for BMCID
PATENT STATUS	LICENSOR
PREPARED BY: DATE:	APPROVED BY: DATE:
J. E. Gajewski April 23, 1974	W. M. Govier 5/15/74

PRODUCT DESCRIPTION, CHARACTERISTICS AND RISKS

To further delineate the neuropharmacologic spectrum especially its usefulness as an anti-anxiety agent in psychotic and neurotic patients alone and in comparison with presently used anxiolytic agents.

SUMMARY OF ANTICIPATED CHALLENGES AND OPPORTUNITIES

Safety and tolerance studies in normal subjects demonstrated that the margin of safety was much higher than predicted from laboratory models. Acute psychotic patients (schizophrenics) showed a tolerance many times greater than normal subjects. Although as a neuroleptic agent, the quantitative response in comparison to presently used agents was low, analysis of the rating scales revealed that relief of anxiety in acute psychotic patients was highly significant, suggesting that perhaps it might be a useful anxiolytic in neurotic patients. Since there are several widely used very efficacious anxiolytic agents available, the costs involved in evaluating this compound as an anxiolytic may not be justified in relationship to the anticipated return if it were marketed.

Probability of Success: 20%

EXHIBIT A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.:	4,182,763
Named Inventors:	George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr.
For:	BUSPIRONE ANTI-ANXIETY METHOD
Issued:	January 8, 1980
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Group Art Unit:	125
Examiner:	Stanley J. Friedman

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

VERIFIED STATEMENT OF FACT AND DECLARATION
OF JOHN E. GAJEWSKI UNDER 37 C.F.R. §1.324

JOHN E. GAJEWSKI states and declares:

1. I, JOHN E. GAJEWSKI, am currently retired and reside at 767 South Hebron Avenue, Evansville, Indiana 47715. Between October 1972 and June 1975 I was employed by the Mead Johnson & Company subsidiary of the Bristol-Myers Company at its facilities in Evansville, Indiana in the capacity of Clinical Associate.

2. I make this statement and declaration in support of the petition to the Commissioner of Patents and Trademarks to correct the inventorship of U.S. Patent No. 4,182,763 by adding my name, John E. Gajewski, as an inventor on the '763 patent.

3. I have read and understood U.S. Patent No. 4,182,763. I have read and understood the Verified

Statements of Fact and Declarations of George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. Under 37 C.F.R. §1.324. I have found no reason to disbelieve any statements made by any and all of them in that document, and based upon my recollection of the facts and the method of doing business at Mead Johnson when I was employed there, I believe that their statements are true.

4. I believe that I am a joint inventor of the invention disclosed and claimed in the '763 patent together with said George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. and as such I believe that my name should be added to the '763 patent as an inventor.

5. My recollection of the facts is as follows:

(a) During the period of 1972 to 1975 my responsibilities included being the clinical monitor for the clinical work being carried out by Dr. Gershon in behalf of Mead Johnson testing the antipsychotic properties of buspirone. This work was reported to Mead Johnson prior to the publication thereof, which I note is mentioned in column 1, lines 47-49 of the '763 patent as, G.L. Sathanathan, et al., Current Therapeutic Research, Vol. 18, (5), pp. 701-705 (1975). "MJ 9022: Correlation Between Neuroleptic Potential and Stereotype."

(b) On about April 23, 1974 I prepared a document in which I suggested a research project to determine the neuropharmacological spectrum of buspirone as an antianxiety agent in neurotic patients, and a comparison be made of buspirone with the then used anxiolytic agents. It was my

stated view that buspirone might be useful as an anxiolytic in neurotic patients. A copy of the document is attached hereto as Exhibit A. The invention of the '763 patent, as defined in the claims is for:

> "A method for the palliative treatment of neurosis in which anxiety symptoms are prominent which comprises administering a non-toxic anxiolytically effective dose of buspirone or a pharmaceutically acceptable acid addition salt thereof to a neurotic patient." (Claim 1).

The dependent claims define inter alia, route of administration and daily dose quantities. I understand that Exhibit A describes the method of at least claim 1 of the '763 patent, particularly by suggesting the usefulness of buspirone as an antianxiety agent in neurotic patient.

(c) To the best of my knowledge and recollection, and in the ordinary course of business practice at Mead Johnson in about 1974, Exhibit A was kept within the administrative areas of Mead Johnson and not submitted either intact or in substance to any of George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. I believe this is true because of my recollection that they were not in the chain of responsibility at Mead Johnson and Bristol-Myers that would have been the basis for any of them receiving a copy of Exhibit A and/or being advised of its existence. I did not advise any of them of the existence of Exhibit A or of its substance.

(d) To the best of my knowledge and recollection, the suggested buspirone project as an antianxiety agent in neurotic patients was never activated during the remainder of my tenure at Mead Johnson.

(e) Between the time that the suggested project was disapproved in about 1974 and the time that I left Mead Johnson in 1975 I am not aware of any work that was done at Mead Johnson in connection with buspirone, other than perhaps some administrative record keeping.

(f) On September 20, 1985 I met with attorneys for the Bristol-Myers Company. They showed me the '763 patent and Exhibit A. They also explained to me the meaning within the context of the U.S. patent laws of "inventorship", and advised me of the requirement for naming all of the inventors on a U.S. patent application and patent.

(g) After reading and understanding these documents, and accepting the advice of the attorneys, I now believe that I am a joint inventor of the invention disclosed and claimed in the '763 patent.

6. After reviewing the facts as set forth above, I now realize and believe that an error was made in failing to include my name as an applicant and joint inventor on S.N. 908,597 and as a joint inventor on the '763 patent, together with the five named inventors currently thereon.

7. I believe that the error in not including my name on S.N. 908,597 was caused by the lack of knowledge by the five named inventors on S.N. 908,597 of the existence of Exhibit A. I believe that the reason that none of the five named inventors saw or knew about Exhibit A prior to the time that it was shown to them, as set forth above in Paragraph 5, and in their Verified Statements of Fact and Declarations is that none of them were in the chain of responsibility at Mead Johnson and Bristol-Myers that would have been the basis for

any of them receiving a copy of Exhibit A and/or being advised of its existence.

8. I do not recall being interviewed by any patent attorneys prior to the time of my interview with the Bristol-Myers attorneys on September 20, 1985 in connection with the buspirone patent matter.

9. In view of the facts as set forth above, and the explanations made to me by the attorneys with respect to the meaning of the term "inventorship," I believe that I am a joint inventor with George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. for the subject matter described and claimed in the '763 patent, and that I was omitted as a named inventor through error. I believe that such error occurred without any deceptive intention by myself or by any of the five named inventors, or anyone else involved with the preparation and prosecution of S.N. 908,597 or anyone else in privy with any of these people, and I have no reason to believe that the error occurred with deceptive intention.

10. I am informed and believe:

(a) That the error without deceptive intention was discovered by one of the attorneys who showed me Exhibit A;

(b) That the attorney had come across document Exhibit A during the course of his review of older Mead Johnson documents (i.e., dated prior to about mid-1975) bearing on busipirone as an antipsychotic agent in connection with his assigned task of reviewing the '763 patent, including

the history of the making of the invention claimed in the '763 patent;

(c) That the review by the attorney was commenced in about late 1984 at which time he began to gather information in aid of his review of the '763 patent;

(d) That Exhibit A was discovered by the attorney in the course of gathering the information in about late 1984;

(e) That the attorney continued his investigation and review of the '763 patent for several more months prior to preparing his report in about April 1985;

(f) That the attorney together with other attorneys of Bristol-Myers thereafter undertook further legal and factual (including further interviews) analyses and considerations on the question of whether I was a joint inventor;

(g) That it was not until about August 1985 that the decision was made to petition the Commissioner of Patents and Trademarks for a Certificate of Correction to add my name as an inventor on the '763 patent; and

(h) That it took about two months to complete the necessary interviews and the necessary papers that were required to prepare the petition for the Certificate of Correction to correct the inventorship of the '763 patent.

11. In view of the facts as set forth above, I believe that it was in about mid-1985 that the error was discovered to exist in fact.

12. Accordingly, I, John E. Gajewski, petition the Commissioner of Patents and Trademarks to correct the

inventorship error and issue a Certificate of Correction that adds the name of John E. Gajewski as an inventor on the '763 patent.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the '763 patent.

Dated: 27 Sept 1995 John E. Gajewski

John E. Gajewski

BRISTOL-MYERS COMPANY
PHARMACEUTICAL, HEALTH CARE, AND INTERNATIONAL GROUP
R & D PROJECT EVALUATION
I - NARRATIVE SUMMARY

PROJECT/~~PROGRAM~~ (6)	B-M DIVISION
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PREPARED BY: DATE:	APPROVED BY: DATE:
J. E. Gajewski April 23, 1974	W. M. Govier 5/15/74

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To further delineate the neuropharmacologic spectrum especially its usefulness as an anti-anxiety agent in psychotic and neurotic patients alone and in comparison with presently used anxiolytic agents.

SUMMARY OF ANTICIPATED CHALLENGES AND OPPORTUNITIES

Safety and tolerance studies in normal subjects demonstrated that the margin of safety was much higher than predicted from laboratory models. Acute psychotic patients (schizophrenics) showed a tolerance many times greater than normal subjects. Although as a neuroleptic agent, the quantitative response in comparison to presently used agents was low, analysis of the rating scales revealed that relief of anxiety in acute psychotic patients was highly significant, suggesting that perhaps it might be a useful anxiolytic in neurotic patients. Since there are several widely used very efficacious anxiolytic agents available, the costs involved in evaluating this compound as an anxiolytic may not be justified in relationship to the anticipated return if it were marketed.

Probability of Success: 20%

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Examiner:	Stanley J. Friedman

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Washington, D.C. 20231

VERIFIED STATEMENT OF FACT AND DECLARATION
OF ROBERT E. CARNAHAN UNDER 37 C.F.R. §1.324

ROBERT E. CARNAHAN states and declares:

1. I, ROBERT E. CARNAHAN, am currently employed by the Bristol-Myers Company at its facilities in Syracuse, New York in the capacity of Director of Patents for the Pharmaceutical and Nutritional Group of the Bristol-Myers Company. In this capacity I am responsible for patent in pharmaceutical and nutritional research. I performed this function for the Mead Johnson & Company subsidiary of Bristol-Myers from 1960 to 1981, and thereafter for Bristol-Myers. Between 1960 and 1981 I was located at the Mead Johnson facilities in Evansville, Indiana, and in 1981 I transferred my office to the Bristol-Myers facilities in Syracuse, New York. I currently reside at 6 Settlers Village, Manlius, New York 13104. I am the Robert E. Carnahan who was given power of attorney by the five named inventors in U.S. Application S.N. 908,597, filed May 22, 1978, and which

application issued as U.S. Patent No. 4,182,763 on January 8, 1980 for "Buspirone Anti-Anxiety Method."

2. I make this statement and declaration in support of the petition to the Commissioner of Patents and Trademarks to correct the inventorship of U.S. Patent No. 4,182,763 by adding the name of John E. Gajewski as an inventor on the '763 patent.

3. I read and understood U.S. Patent No. 4,182,763. I read and understood the Verified Statements of Fact and Declarations of George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. Under 37 C.F.R. §1.324. I found no reason to disbelieve any statements made by any and all of them in that document, and based upon my recollection of the facts and the method of doing business at Mead Johnson when I was there, I believe that their statements are true.

4. In about early 1978 I was advised that a new use for buspirone had been invented and that my advice was sought with respect to the patentability of the new use. I met with George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel Jr. and discussed with them the nature of the new invention and reached the conclusion that the new use for buspirone was patentable. The new use in terms of the claims of the '763 patent was:

> "A method for the palliative treatment of neurosis in which anxiety symptoms are prominent which comprises administering a non-toxic anxiolytically effective dose of buspirone or a pharmaceutically acceptable acid addition salt thereof to a neurotic patient." (Claim 1.)

The dependent claims define, inter alia, route of administration and daily dose quantities.

5. I discussed the invention with the five named inventors and reviewed documents contemporaneous with the time of their making the invention and thereafter. I also reviewed certain earlier documents, including documents that described early animal work with buspirone when it was being tested as an antipsychotic agent. As mentioned hereinafter, I did not see document Exhibit A during that review.

6. Based upon my review and discussions, as set forth above, I reached the conclusion that the new use for buspirone was patentable in the United States and that the five named inventors were joint inventors of that invention. I thereupon prepared an application disclosing and claiming that invention and also prepared a declaration for the five inventors and forwarded the same to them. Each of the five named inventors signed the declaration, and the application was filed in their names on May 22, 1978.

7. I continued to believe that the five named inventors were the only joint inventors of the invention of the '763 patent until the time I was shown a document that was prepared by Dr. John E. Gajewski. [Attached hereto as Exhibit A.] The date of that document (April 23, 1974) was prior to the time that the five named inventors made the invention of the '763 patent (about mid-1975) and prior to the time that I discussed the invention with them (about 1977 and early 1978), and prepared and filed the application for the invention.

8. My recollection of the facts is as follows:

(a) The first time I saw Exhibit A was in about the early part of 1985;

(b) I did not know of the existence of Exhibit A prior to the first time that I saw it;

(c) I did not know that Dr. Gajewski had prepared Exhibit A prior to the first time that I saw it;

(d) I did not interview Dr. Gajewski in connection with the new use of buspirone;

(e) I was shown Exhibit A for the first time by an attorney for Bristol-Myers;

(f) I discussed with the attorney the meaning, within the context of the U.S. patent laws, of "inventorship," and also discussed with the attorney the requirements for naming all inventors on a U.S. patent application and patent; and

(g) After reading and understanding Exhibit A, and in view of the discussions I had with the attorney, I now believe that Dr. Gajewski is a joint inventor of the invention disclosed and claimed in the '763 patent.

9. I read and understood the Statement of Fact and Declaration of John E. Gajewski and now realize and believe that an error was made in failing to include Dr. Gajewski as an applicant and joint inventor on S.N. 908,597 and as a joint inventor on the '763 patent together with the five named inventors.

10. I believe that the error in not including Dr. Gajewski on S.N. 908,597 was caused by the lack of knowledge by the five named inventors and myself of the

existence of Exhibit A. I believe that the reason that none of the five named inventors and I did not know about Exhibit A prior to the time it was shown to each of us as set forth above in Paragraph 8, is that none of us were in the chain of responsibility at Mead Johnson and Bristol-Myers that would have been the basis for any of us to receive a copy of Exhibit A and/or being advised of its existence.

11. I understand that Exhibit A describes the concept of the method of at least claim 1 of the '763 patent particularly by suggesting the usefulness of buspirone as an antianxiety agent in neurotic patients.

12. In view of the facts as set forth above, and my understanding of the patent law with respect to the meaning of the term "inventorship," I believe that Dr. Gajewski is a joint inventor together with the five named inventors for the subject matter described and claimed in the '763 patent, and that Dr. Gajewski was omitted as a named inventor through error. I believe that such error occurred without any deceptive intention by any of the five named inventors, or Dr. Gajewski, or myself, or anyone else involved with the preparation and prosecution of S.N. 908,597 or anyone else in privy with any of these people, and I have no reason to believe that the error occurred with deceptive intention.

13. In about the latter part of 1984, the Bristol-Myers Company caused a review of the '763 patent to be undertaken by one of its counsel, who, I believe, previous to such undertaking had no contact with the '763 patent and/or its preparation or the making of the invention thereof. The

counsel, on information and belief, undertook to investigate and review in depth, the relevant records of the Mead Johnson & Company subsidiary of Bristol-Myers and of the Bristol-Myers Company, as well as conducting interviews with the named inventors and others having information with respect to the invention. I believe that in the course of such investigation the counsel found Exhibit A, and in the course of further investigations and legal analyses reached the conclusion that Dr. Gajewski was a joint inventor together with the five named inventors, and that Dr. Gajewski's name was omitted from S.N. 908,597 and from the '763 patent in error and without deceptive intention. I believe that upon reporting his findings in about April 1985, further investigations and interviews were conducted, and as a consequence thereof, a decision was made that correction of the named inventors under 35 U.S.C. §256 was proper and should be sought. I believe that the period of investigation, review, consideration, interview and decision of what action should be taken began during the later part of 1984 and lasted through September 1985. Taking into consideration the scope of the original undertaking and the complex factual and legal nature of this situation, it is believed, and it is respectfully submitted that elapsed time was entirely reasonable and that the petition for a Certificate of Correction is being diligently and timely made.

14. I am informed and believe:

(a) That the error without deceptive intention was discovered by one of the attorneys who first showed me Exhibit A;

(b) That the attorney had come across document Exhibit A during the course of his review of older Mead Johnson documents (i.e., dated prior to about mid-1975) bearing on busipirone as an antipsychotic agent in connection with his assigned task of reviewing the '763 patent, including the history of the making of the invention claimed in the '763 patent;

(c) That the review by the attorney was commenced in about late 1984 at which time he began to gather information in aid of his review of the '763 patent;

(d) That Exhibit A was discovered by the attorney in the course of gathering the information in about late 1984;

(e) That the attorney continued his investigation and review of the '763 patent for several more months prior to preparing his report in about April 1985;

(f) That the attorney together with other attorneys of Bristol-Myers thereafter undertook further legal and factual (including further interviews) analyses and considerations on the question of whether Dr. Gajewski was a joint inventor;

(g) That it was not until about August 1985 that the decision was made to petition the Commissioner of Patents and Trademarks for a Certificate of Correction to add the name of Dr. Gajewski as an inventor on the '763 patent; and

(h) That it took about two months to complete the necessary interviews and the necessary papers that were required to prepare the petition for the Certificate of Correction to correct the inventorship of the '763 patent.

15. In view of the facts as set forth above, I believe that it was in about mid-1985 that the error was discovered to exist in fact.

16. Accordingly, I request that the Commissioner of Patents and Trademarks correct the inventorship error by granting the petition to issue a Certificate of Correction that adds the name of John E. Gajewski as an inventor on the '763 patent.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the '763 patent,

Dated: Sep 25 '85 Robert E. Carnahan

Robert E. Carnahan

BRISTOL-MYERS COMPANY
PHARMACEUTICAL, HEALTH CARE, AND INTERNATIONAL GROUP
R & D PROJECT EVALUATION
I - NARRATIVE SUMMARY

PROJECT/~~PROGRAM~~ (6)	B-M DIVISION
Buspirone - Project 9022	Mead Johnson and Company for BMCID
PATENT STATUS	LICENSOR
PREPARED BY: DATE:	APPROVED BY: DATE:
J. E. Gajewski April 23, 1974	W. M. Govier 5/15/74

PRODUCT DESCRIPTION, CHARACTERISTICS AND RISKS

To further delineate the neuropharmacologic spectrum especially its usefulness as an anti-anxiety agent in psychotic and neurotic patients alone and in comparison with presently used anxiolytic agents.

SUMMARY OF ANTICIPATED CHALLENGES AND OPPORTUNITIES

Safety and tolerance studies in normal subjects demonstrated that the margin of safety was much higher than predicted from laboratory models. Acute psychotic patients (schizophrenics) showed a tolerance many times greater than normal subjects. Although as a neuroleptic agent, the quantitative response in comparison to presently used agents was low, analysis of the rating scales revealed that relief of anxiety in acute psychotic patients was highly significant, suggesting that perhaps it might be a useful anxiolytic in neurotic patients. Since there are several widely used very efficacious anxiolytic agents available, the costs involved in evaluating this compound as an anxiolytic may not be justified in relationship to the anticipated return if it were marketed.

Probability of Success: 20%

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.:	4,182,763
Named Inventors:	George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr.
For:	BUSPIRONE ANTI-ANXIETY METHOD
Issued:	January 8, 1980
Serial No.:	908,597
Filed:	May 22, 1978
Group Art Unit:	125
Examiner:	Stanley J. Friedman

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

DECLARATION, POWER OF ATTORNEY AND PETITION
UNDER 37 C.F.R. §1.63
FOR APPLICATION S.N. 908,597 NOW
U.S. PATENT NO. 4,182,763

We, GEORGE P. CASTEN, GORDON R. McKINNEY, ROGER E. NEWTON, E. CROSBY TOMPKINS, JOHN H. WEIKEL, JR. and JOHN E. GAJEWSKI declare as follows:

1. I, GEORGE P. CASTEN, declare that I am a citizen of the United States of America residing at 7416 Adams Avenue, Evansville, Indiana 47715.

2. I, GORDON R. McKINNEY, declare that I am a citizen of the United States of America residing at 421 Kings Valley Road, Evansville, Indiana 47711.

3. I, ROGER E. NEWTON, declare that I am a citizen of the United States of America residing at 1400 Lark Drive, Evansville, Indiana 47715.

4. I, E. CROSBY TOMPKINS, declare that I am a citizen of the United States of America residing at 15119 Fairmont Court, Grand Haven, Michigan 49417.

5. I, JOHN R. WEIKEL, JR., declare that I am a citizen of the United States of America residing at R.R. #4, Box 266, Mount Vernon, Indiana 47620.

6. I, JOHN E. GAJEWSKI, declare that I am a citizen of the United States of America residing at 767 South Hebron Avenue, Evansville, Indiana 47715.

7. We each verily believe that we are the original, first and joint inventors of the invention entitled "Buspirone Anti-Anxiety Method," described and claimed in the specification filed May 22, 1978 as Application Serial No. 908,597 that was issued as U.S. Patent No. 4,182,763 on January 8, 1980; that we each reviewed and understand the contents of said application and patent; that, as to the subject matter of this application and patent, we each do not know and do not believe that this invention was ever known or used in the United States of America before our invention thereof, or patented or made the subject of an inventor's certificate or described in any printed publication in any country before our invention thereof, or more than one year prior to May 22, 1978; or in public use or on sale in the United States of America more than one year prior to May 22, 1978; that the said subject matter has not been patented or made the subject of an inventor's certificate before May 22, 1978 in any country foreign to the United States on an application filed by us or our legal representatives or

assigns more than twelve months before May 22, 1978; that we each acknowledge our duty to disclose information of which we each are aware which is material to the examination of this application; and that no application for patent or an inventor's certificate on said subject matter has been filed by us or our representatives or assigns in any country foreign to the United States of America prior to May 22, 1978.

8. We hereby appoint Robert E. Carnahan, Registration No. 18,500, Bristol Laboratories, Bristol-Myers Company, P.O. Box 4755, Syracuse, New York 13221-4755, Telephone No. (315) 432-4813, our agent with full power of substitution and revocation, to prosecute the petition for Certificate of Correction and to transact all business in the Patent and Trademark Office connected therewith. Please address all communications to Dr. Carnahan.

9. Wherefore we pray that said U.S. Patent No. 4,182,763 be corrected to add the name of John E. Gajewski as an inventor of said U.S. Patent No. 4,182,763.

10. We make this Declaration, Power of Attorney and Petition under 37 C.F.R. §1.63 For Application S.N. 908,597 now U.S. Patent No. 4,182,763 in support of the Petition Under 37 C.F.R. §1.324 to correct inventorship by adding the name of John E. Gajewski as an inventor on U.S. Patent No. 4,182,763, and we hereby subscribe our names to this Declaration, Power of Attorney and Petition under 37 C.F.R. §1.63 For Application S.N. 908,597 now U.S. Patent No. 4,182,763.

We, the undersigned, declare further that all statements herein of our own knowledge are true and that all

statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of U.S. Patent No. 4,182,763.

Inventor's Name and Signature: George P. Casten
George P. Casten

Date: 9-26-85

Post Office Address: 7416 Adams Avenue
Evansville, Indiana 47715

Inventor's Name and Signature: Gordon R. McKinney
Gordon R. McKinney

Date: Sept. 27, 1985

Post Office Address: 421 Kings Valley Road
Evansville, Indiana 47711

Inventor's Name and Signature: Roger E. Newton
Roger E. Newton

Date: September 25, 1985

Post Office Address: 1400 Lark Drive
Evansville, Indiana 47715

Inventor's Name and Signature: E. Crosby Tompkins
E. Crosby Tompkins

Date: September 30, 1985

Post Office Address: 15119 Fairmont Court
Grand Haven, Michigan 49417

Inventor's Name and Signature: John N. Weikel, Jr.
John N. Weikel, Jr.

Date: Sept. 26, 1985

Post Office Address: R.R. #4, Box 266
Mount Vernon, Indiana 47620

Inventor's Name and Signature: John E. Gajewski

Date: 27 Sept 1985

Post Office Address: 767 South Hebron Avenue
Evansville, Indiana 4771

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.:	4,182,763
Named Inventors:	George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr.
For:	BUSPIRONE ANTI-ANXIETY METHOD
Issued:	January 8, 1980
Serial No.:	908,597
Filed:	May 22, 1978
Group Art Unit:	125
Examiner:	Stanley J. Friedman

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

CONSENT OF ASSIGNEE

Sir:

The assignee of record for U.S. Patent No. 4,182,763, Mead Johnson & Company, hereby consents to the addition of the name of John E. Gajewski as an inventor of said U.S. Patent No. 4,182,763.

MEAD JOHNSON & COMPANY

Dated: October 1, 1985

By J. R. Edmondson
Officer
J. R. Edmondson
Vice President

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.:	4,182,763
Named Inventors:	George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr.
For:	BUSPIRONE ANTI-ANXIETY METHOD
Issued:	January 8, 1980
Serial No.:	908,597
Filed:	May 22, 1978
Group Art Unit:	125
Examiner:	Stanley J. Friedman

Duplicate

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

VERIFIED STATEMENT OF FACT AND DECLARATION
OF ROBERT E. CARNAHAN UNDER 37 C.F.R. §1.324

ROBERT E. CARNAHAN states and declares:

1. I, ROBERT E. CARNAHAN, am currently employed by the Bristol-Myers Company at its facilities in Syracuse, New York in the capacity of Director of Patents for the Pharmaceutical and Nutritional Group of the Bristol-Myers Company. In this capacity I am responsible for patent in pharmaceutical and nutritional research. I performed this function for the Mead Johnson & Company subsidiary of Bristol-Myers from 1960 to 1981, and thereafter for Bristol-Myers. Between 1960 and 1981 I was located at the Mead Johnson facilities in Evansville, Indiana, and in 1981 I transferred my office to the Bristol-Myers facilities in Syracuse, New York. I currently reside at 6 Settlers Village, Manlius, New York 13104. I am the Robert E. Carnahan who was given power of attorney by the five named inventors in U.S. Application S.N. 908,597, filed May 22, 1978, and which

application issued as U.S. Patent No. 4,182,763 on January 8, 1980 for "Buspirone Anti-Anxiety Method."

2. I make this statement and declaration in support of the petition to the Commissioner of Patents and Trademarks to correct the inventorship of U.S. Patent No. 4,182,763 by adding the name of John E. Gajewski as an inventor on the '763 patent.

3. I read and understood U.S. Patent No. 4,182,763. I read and understood the Verified Statements of Fact and Declarations of George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. Under 37 C.F.R. §1.324. I found no reason to disbelieve any statements made by any and all of them in that document, and based upon my recollection of the facts and the method of doing business at Mead Johnson when I was there, I believe that their statements are true.

4. In about early 1978 I was advised that a new use for buspirone had been invented and that my advice was sought with respect to the patentability of the new use. I met with George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel Jr. and discussed with them the nature of the new invention and reached the conclusion that the new use for buspirone was patentable. The new use in terms of the claims of the '763 patent was:

> "A method for the palliative treatment of neurosis in which anxiety symptoms are prominent which comprises administering a non-toxic anxiolytically effective dose of buspirone or a pharmaceutically acceptable acid addition salt thereof to a neurotic patient." (Claim 1.)

The dependent claims define, inter alia, route of administration and daily dose quantities.

5. I discussed the invention with the five named inventors and reviewed documents contemporaneous with the time of their making the invention and thereafter. I also reviewed certain earlier documents, including documents that described early animal work with buspirone when it was being tested as an antipsychotic agent. As mentioned hereinafter, I did not see document Exhibit A during that review.

6. Based upon my review and discussions, as set forth above, I reached the conclusion that the new use for buspirone was patentable in the United States and that the five named inventors were joint inventors of that invention. I thereupon prepared an application disclosing and claiming that invention and also prepared a declaration for the five inventors and forwarded the same to them. Each of the five named inventors signed the declaration, and the application was filed in their names on May 22, 1978.

7. I continued to believe that the five named inventors were the only joint inventors of the invention of the '763 patent until the time I was shown a document that was prepared by Dr. John E. Gajewski. [Attached hereto as Exhibit A.] The date of that document (April 23, 1974) was prior to the time that the five named inventors made the invention of the '763 patent (about mid-1975) and prior to the time that I discussed the invention with them (about 1977 and early 1978), and prepared and filed the application for the invention.

8. My recollection of the facts is as follows:

(a) The first time I saw Exhibit A was in about the early part of 1985;

(b) I did not know of the existence of Exhibit A prior to the first time that I saw it;

(c) I did not know that Dr. Gajewski had prepared Exhibit A prior to the first time that I saw it;

(d) I did not interview Dr. Gajewski in connection with the new use of buspirone;

(e) I was shown Exhibit A for the first time by an attorney for Bristol-Myers;

(f) I discussed with the attorney the meaning, within the context of the U.S. patent laws, of "inventorship," and also discussed with the attorney the requirements for naming all inventors on a U.S. patent application and patent; and

(g) After reading and understanding Exhibit A, and in view of the discussions I had with the attorney, I now believe that Dr. Gajewski is a joint inventor of the invention disclosed and claimed in the '763 patent.

9. I read and understood the Statement of Fact and Declaration of John E. Gajewski and now realize and believe that an error was made in failing to include Dr. Gajewski as an applicant and joint inventor on S.N. 908,597 and as a joint inventor on the '763 patent together with the five named inventors.

10. I believe that the error in not including Dr. Gajewski on S.N. 908,597 was caused by the lack of knowledge by the five named inventors and myself of the

existence of Exhibit A. I believe that the reason that none of the five named inventors and I did not know about Exhibit A prior to the time it was shown to each of us as set forth above in Paragraph 8, is that none of us were in the chain of responsibility at Mead Johnson and Bristol-Myers that would have been the basis for any of us to receive a copy of Exhibit A and/or being advised of its existence.

11. I understand that Exhibit A describes the concept of the method of at least claim 1 of the '763 patent particularly by suggesting the usefulness of buspirone as an antianxiety agent in neurotic patients.

12. In view of the facts as set forth above, and my understanding of the patent law with respect to the meaning of the term "inventorship," I believe that Dr. Gajewski is a joint inventor together with the five named inventors for the subject matter described and claimed in the '763 patent, and that Dr. Gajewski was omitted as a named inventor through error. I believe that such error occurred without any deceptive intention by any of the five named inventors, or Dr. Gajewski, or myself, or anyone else involved with the preparation and prosecution of S.N. 908,597 or anyone else in privy with any of these people, and I have no reason to believe that the error occurred with deceptive intention.

13. In about the latter part of 1984, the Bristol-Myers Company caused a review of the '763 patent to be undertaken by one of its counsel, who, I believe, previous to such undertaking had no contact with the '763 patent and/or its preparation or the making of the invention thereof. The

counsel, on information and belief, undertook to investigate and review in depth, the relevant records of the Mead Johnson & Company subsidiary of Bristol-Myers and of the Bristol-Myers Company, as well as conducting interviews with the named inventors and others having information with respect to the invention. I believe that in the course of such investigation the counsel found Exhibit A, and in the course of further investigations and legal analyses reached the conclusion that Dr. Gajewski was a joint inventor together with the five named inventors, and that Dr. Gajewski's name was omitted from S.N. 908,597 and from the '763 patent in error and without deceptive intention. I believe that upon reporting his findings in about April 1985, further investigations and interviews were conducted, and as a consequence thereof, a decision was made that correction of the named inventors under 35 U.S.C. §256 was proper and should be sought. I believe that the period of investigation, review, consideration, interview and decision of what action should be taken began during the later part of 1984 and lasted through September 1985. Taking into consideration the scope of the original undertaking and the complex factual and legal nature of this situation, it is believed, and it is respectfully submitted that elapsed time was entirely reasonable and that the petition for a Certificate of Correction is being diligently and timely made.

14. I am informed and believe:

(a) That the error without deceptive intention was discovered by one of the attorneys who first showed me Exhibit A;

(b) That the attorney had come across document Exhibit A during the course of his review of older Mead Johnson documents (i.e., dated prior to about mid-1975) bearing on busipirone as an antipsychotic agent in connection with his assigned task of reviewing the '763 patent, including the history of the making of the invention claimed in the '763 patent;

(c) That the review by the attorney was commenced in about late 1984 at which time he began to gather information in aid of his review of the '763 patent;

(d) That Exhibit A was discovered by the attorney in the course of gathering the information in about late 1984;

(e) That the attorney continued his investigation and review of the '763 patent for several more months prior to preparing his report in about April 1985;

(f) That the attorney together with other attorneys of Bristol-Myers thereafter undertook further legal and factual (including further interviews) analyses and considerations on the question of whether Dr. Gajewski was a joint inventor;

(g) That it was not until about August 1985 that the decision was made to petition the Commissioner of Patents and Trademarks for a Certificate of Correction to add the name of Dr. Gajewski as an inventor on the '763 patent; and

(h) That it took about two months to complete the necessary interviews and the necessary papers that were required to prepare the petition for the Certificate of Correction to correct the inventorship of the '763 patent.

15. In view of the facts as set forth above, I believe that it was in about mid-1985 that the error was discovered to exist in fact.

16. Accordingly, I request that the Commissioner of Patents and Trademarks correct the inventorship error by granting the petition to issue a Certificate of Correction that adds the name of John E. Gajewski as an inventor on the '763 patent.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the '763 patent,

Dated: Sep 25 '85 Robert E. Carnahan

Robert E. Carnahan

BRISTOL-MYERS COMPANY
PHARMACEUTICAL, HEALTH CARE, AND INTERNATIONAL GROUP
R & D PROJECT EVALUATION
I - NARRATIVE SUMMARY

PROJECT/~~PROGRAM~~ (6)	B-M DIVISION
Buspirone - Project 9022	Mead Johnson and Company for BMCID
PATENT STATUS	LICENSOR
PREPARED BY: DATE:	APPROVED BY: DATE:
J. E. Gajewski April 23, 1974	W. M. Govier 5/15/74

PRODUCT DESCRIPTION, CHARACTERISTICS AND RISKS

To further delineate the neuropharmacologic spectrum especially its usefulness as an anti-anxiety agent in psychotic and neurotic patients alone and in comparison with presently used anxiolytic agents.

SUMMARY OF ANTICIPATED CHALLENGES AND OPPORTUNITIES

Safety and tolerance studies in normal subjects demonstrated that the margin of safety was much higher than predicted from laboratory models. Acute psychotic patients (schizophrenics) showed a tolerance many times greater than normal subjects. Although as a neuroleptic agent, the quantitative response in comparison to presently used agents was low, analysis of the rating scales revealed that relief of anxiety in acute psychotic patients was highly significant, suggesting that perhaps it might be a useful anxiolytic in neurotic patients. Since there are several widely used very efficacious anxiolytic agents available, the costs involved in evaluating this compound as an anxiolytic may not be justified in relationship to the anticipated return if it were marketed.

Probability of Success: 20%

EXHIBIT A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.:	4,182,763
Named Inventors:	George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr.
For:	BUSPIRONE ANTI-ANXIETY METHOD
Issued:	January 8, 1980
Serial No.:	908,597
Filed:	May 22, 1978
Group Art Unit:	125
Examiner:	Stanley J. Friedman

Duplicate

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

VERIFIED STATEMENT OF FACT AND DECLARATION
OF JOHN E. GAJEWSKI UNDER 37 C.F.R. §1.324

JOHN E. GAJEWSKI states and declares:

1. I, JOHN E. GAJEWSKI, am currently retired and reside at 767 South Hebron Avenue, Evansville, Indiana 47715. Between October 1972 and June 1975 I was employed by the Mead Johnson & Company subsidiary of the Bristol-Myers Company at its facilities in Evansville, Indiana in the capacity of Clinical Associate.

2. I make this statement and declaration in support of the petition to the Commissioner of Patents and Trademarks to correct the inventorship of U.S. Patent No. 4,182,763 by adding my name, John E. Gajewski, as an inventor on the '763 patent.

3. I have read and understood U.S. Patent No. 4,182,763. I have read and understood the Verified

Statements of Fact and Declarations of George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. Under 37 C.F.R. §1.324. I have found no reason to disbelieve any statements made by any and all of them in that document, and based upon my recollection of the facts and the method of doing business at Mead Johnson when I was employed there, I believe that their statements are true.

4. I believe that I am a joint inventor of the invention disclosed and claimed in the '763 patent together with said George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. and as such I believe that my name should be added to the '763 patent as an inventor.

5. My recollection of the facts is as follows:

(a) During the period of 1972 to 1975 my responsibilities included being the clinical monitor for the clinical work being carried out by Dr. Gershon in behalf of Mead Johnson testing the antipsychotic properties of buspirone. This work was reported to Mead Johnson prior to the publication thereof, which I note is mentioned in column 1, lines 47-49 of the '763 patent as, G.L. Sathanathan, et al., Current Therapeutic Research, Vol. 18, (5), pp. 701-705 (1975). "MJ 9022: Correlation Between Neuroleptic Potential and Stereotype."

(b) On about April 23, 1974 I prepared a document in which I suggested a research project to determine the neuropharmacological spectrum of buspirone as an antianxiety agent in neurotic patients, and a comparison be made of buspirone with the then used anxiolytic agents. It was my

stated view that buspirone might be useful as an anxiolytic in neurotic patients. A copy of the document is attached hereto as Exhibit A. The invention of the '763 patent, as defined in the claims is for:

> "A method for the palliative treatment of neurosis in which anxiety symptoms are prominent which comprises administering a non-toxic anxiolytically effective dose of buspirone or a pharmaceutically acceptable acid addition salt thereof to a neurotic patient." (Claim 1).

The dependent claims define inter alia, route of administration and daily dose quantities. I understand that Exhibit A describes the method of at least claim 1 of the '763 patent, particularly by suggesting the usefulness of buspirone as an antianxiety agent in neurotic patient.

(c) To the best of my knowledge and recollection, and in the ordinary course of business practice at Mead Johnson in about 1974, Exhibit A was kept within the administrative areas of Mead Johnson and not submitted either intact or in substance to any of George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. I believe this is true because of my recollection that they were not in the chain of responsibility at Mead Johnson and Bristol-Myers that would have been the basis for any of them receiving a copy of Exhibit A and/or being advised of its existence. I did not advise any of them of the existence of Exhibit A or of its substance.

(d) To the best of my knowledge and recollection, the suggested buspirone project as an antianxiety agent in neurotic patients was never activated during the remainder of my tenure at Mead Johnson.

(e) Between the time that the suggested project was disapproved in about 1974 and the time that I left Mead Johnson in 1975 I am not aware of any work that was done at Mead Johnson in connection with buspirone, other than perhaps some administrative record keeping.

(f) On September 20, 1985 I met with attorneys for the Bristol-Myers Company. They showed me the '763 patent and Exhibit A. They also explained to me the meaning within the context of the U.S. patent laws of "inventorship", and advised me of the requirement for naming all of the inventors on a U.S. patent application and patent.

(g) After reading and understanding these documents, and accepting the advice of the attorneys, I now believe that I am a joint inventor of the invention disclosed and claimed in the '763 patent.

6. After reviewing the facts as set forth above, I now realize and believe that an error was made in failing to include my name as an applicant and joint inventor on S.N. 908,597 and as a joint inventor on the '763 patent, together with the five named inventors currently thereon.

7. I believe that the error in not including my name on S.N. 908,597 was caused by the lack of knowledge by the five named inventors on S.N. 908,597 of the existence of Exhibit A. I believe that the reason that none of the five named inventors saw or knew about Exhibit A prior to the time that it was shown to them, as set forth above in Paragraph 5, and in their Verified Statements of Fact and Declarations is that none of them were in the chain of responsibility at Mead Johnson and Bristol-Myers that would have been the basis for

any of them receiving a copy of Exhibit A and/or being advised of its existence.

8. I do not recall being interviewed by any patent attorneys prior to the time of my interview with the Bristol-Myers attorneys on September 20, 1985 in connection with the buspirone patent matter.

9. In view of the facts as set forth above, and the explanations made to me by the attorneys with respect to the meaning of the term "inventorship," I believe that I am a joint inventor with George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr. for the subject matter described and claimed in the '763 patent, and that I was omitted as a named inventor through error. I believe that such error occurred without any deceptive intention by myself or by any of the five named inventors, or anyone else involved with the preparation and prosecution of S.N. 908,597 or anyone else in privy with any of these people, and I have no reason to believe that the error occurred with deceptive intention.

10. I am informed and believe:

(a) That the error without deceptive intention was discovered by one of the attorneys who showed me Exhibit A;

(b) That the attorney had come across document Exhibit A during the course of his review of older Mead Johnson documents (i.e., dated prior to about mid-1975) bearing on busipirone as an antipsychotic agent in connection with his assigned task of reviewing the '763 patent, including

the history of the making of the invention claimed in the '763 patent;

(c) That the review by the attorney was commenced in about late 1984 at which time he began to gather information in aid of his review of the '763 patent;

(d) That Exhibit A was discovered by the attorney in the course of gathering the information in about late 1984;

(e) That the attorney continued his investigation and review of the '763 patent for several more months prior to preparing his report in about April 1985;

(f) That the attorney together with other attorneys of Bristol-Myers thereafter undertook further legal and factual (including further interviews) analyses and considerations on the question of whether I was a joint inventor;

(g) That it was not until about August 1985 that the decision was made to petition the Commissioner of Patents and Trademarks for a Certificate of Correction to add my name as an inventor on the '763 patent; and

(h) That it took about two months to complete the necessary interviews and the necessary papers that were required to prepare the petition for the Certificate of Correction to correct the inventorship of the '763 patent.

11. In view of the facts as set forth above, I believe that it was in about mid-1985 that the error was discovered to exist in fact.

12. Accordingly, I, John E. Gajewski, petition the Commissioner of Patents and Trademarks to correct the

inventorship error and issue a Certificate of Correction that adds the name of John E. Gajewski as an inventor on the '763 patent.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the '763 patent.

Dated: 27 Sept 1995 John E. Gajewski

John E. Gajewski

BRISTOL-MYERS COMPANY
PHARMACEUTICAL, HEALTH CARE, AND INTERNATIONAL GROUP
R & D PROJECT EVALUATION
I - NARRATIVE SUMMARY

PROJECT/~~PROGRAM~~ (6)	B-M DIVISION
Buspirone - Project 9022	Mead Johnson and Company for BMCID
PATENT STATUS	LICENSOR
PREPARED BY: DATE:	APPROVED BY: DATE:
J. E. Gajewski April 23, 1974	W. M. Govier 5/15/74

PRODUCT DESCRIPTION, CHARACTERISTICS AND RISKS

To further delineate the neuropharmacologic spectrum especially its usefulness as an anti-anxiety agent in psychotic and neurotic patients alone and in comparison with presently used anxiolytic agents.

SUMMARY OF ANTICIPATED CHALLENGES AND OPPORTUNITIES

Safety and tolerance studies in normal subjects demonstrated that the margin of safety was much higher than predicted from laboratory models. Acute psychotic patients (schizophrenics) showed a tolerance many times greater than normal subjects. Although as a neuroleptic agent, the quantitative response in comparison to presently used agents was low, analysis of the rating scales revealed that relief of anxiety in acute psychotic patients was highly significant, suggesting that perhaps it might be a useful anxiolytic in neurotic patients. Since there are several widely used very efficacious anxiolytic agents available, the costs involved in evaluating this compound as an anxiolytic may not be justified in relationship to the anticipated return if it were marketed.

Probability of Success: 20%

EXHIBIT A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.:	4,182,763
Named Inventors:	George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr.
For:	BUSPIRONE ANTI-ANXIETY METHOD
Issued:	January 8, 1980
Serial No.:	908,597
Filed:	May 22, 1978
Group Art Unit:	125
Examiner:	Stanley J. Friedman

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

VERIFIED STATEMENTS OF FACT AND DECLARATIONS OF GEORGE P. CASTEN, GORDON R. McKINNEY, ROGER E. NEWTON, E. CROSBY TOMPKINS AND JOHN H. WEIKEL, JR. UNDER 37 C.F.R. §1.324

GEORGE P. CASTEN, GORDON R. McKINNEY, ROGER E. NEWTON, E. CROSBY TOMPKINS AND JOHN H. WEIKEL, JR. (hereinafter referred to jointly as the "named inventors") state and declare, individually as indicated and jointly as indicated:

1. I, GEORGE P. CASTEN, am the named GEORGE P. CASTEN, one of the named inventors on U.S. Patent No. 4,182,763 that was issued on January 8, 1980 and is entitled "Buspirone Anti-Anxiety Method." I am currently employed by the Pharmaceutical Research and Development Division of the Bristol-Myers Company at its facilities in Evansville, Indiana in the capacity of Senior Research Scientist and have been so employed in this capacity since 1982. At all prior relevant times herein I was employed in a similar capacity by the Mead Johnson & Company subsidiary of the Bristol-Myers Company in

Evansville, and specifically between 1971 and 1978 I was involved in the regulatory affairs of Mead Johnson and between 1978 and 1982 I became a Senior Research Scientist of Mead Johnson. I currently reside at 7416 Adams Avenue, Evansville, Indiana 47715.

2. I, GORDON R. McKINNEY, am the named GORDON R. McKINNEY, one of the named inventors on U.S. Patent No. 4,182,763 that was issued on January 8, 1980 and is entitled "Buspirone Anti-Anxiety Method." I am currently employed by the Mead Johnson & Company subsidiary of the Bristol-Myers Company at its facilities in Evansville, Indiana in the capacity of Director of Medical Communications and have been employed in this capacity since 1980. Prior to 1980 and at all relevant times herein I was employed by Mead Johnson in Evansville, ~~to perform the same function, and~~ specifically between 1968 and 1975 I was the Director of Pharmacology, between 1975 and 1978 I was the Director of Biological Research, and between 1978 and 1980 I was the Associate Director of Medical Services. I currently reside at 421 Kings Valley Road, Evansville, Indiana 47711.

Gordon R. McKinney Sept. 27, 1985

3. I, ROGER E. NEWTON, am the named ROGER E. NEWTON, one of the named inventors on U.S. Patent No. 4,182,763 that was issued on January 8, 1980 and is entitled "Buspirone Anti-Anxiety Method." I am currently a consultant to the Pharmaceutical Research and Development Division of the Bristol-Myers Company. During the period between May 1966 and 1982 I was employed by the Mead Johnson & Company subsidiary of the Bristol-Myers Company in Evansville, Indiana, and between 1982 and 1984 I was employed by the Pharmaceutical

Research and Development Division of the Bristol-Myers Company in Evansville in the capacity of Associate Medical Director and Director of Clinical Research. I currently reside at 1400 Lark Drive, Evansville, Indiana 47715.

4. I, E. CROSBY TOMPKINS, am the named E. CROSBY TOMPKINS, one of the named inventors on U.S. Patent No. 4,182,763 that was issued on January 8, 1980 and is entitled "Buspirone Anti-Anxiety Method." I am currently employed by Toxicity Research Laboratories in its facilities in Muskegon, Michigan in the capacity of Vice President and Director of Toxicology since 1978. I was employed by the Mead Johnson & Company subsidiary of the Bristol-Myers Company in 1970 as a Senior Investigator and in 1978 I became a Principal Investigator. I was employed at the Mead Johnson facilities in Evansville, Indiana. In 1978 I left the employ of Mead Johnson and became employed by Toxicity Research Laboratories. I currently reside at 15119 Fairmont Court, Grand Haven, Michigan 49417.

5. I, JOHN H. WEIKEL, JR., am the named JOHN H. WEIKEL, JR., one of the named inventors on U.S. Patent No. 4,182,763 that was issued on January 8, 1980 and is entitled "Buspirone Anti-Anxiety Method." I am currently employed by the Pharmaceutical Research and Development Division of the Bristol-Myers Company at its facilities in Evansville, Indiana in the capacity of Director of Pathology and Toxicology and have been so employed at all relevant times herein. Prior to 1982 I was employed in a similar capacity by the Mead Johnson & Company subsidiary of the Bristol-Myers Company in

Evansville. I currently reside at R.R. #4, Box 266, Mount Vernon, Indiana 47620.

6. The named inventors make this statement and declaration in support of the petition to the Commissioner of Patents and Trademarks to correct the inventorship of U.S. Patent No. 4,182,763 by adding the name of John E. Gajewski as an inventor on the '763 patent.

7. At the time that the named inventors signed the declaration for said S.N. 908,597, they believed, individually and jointly, that they, and only they, jointly made the invention disclosed and claimed in said S.N. 908,597. The invention, as defined in the claims is for:

> "A method for the palliative treatment of neurosis in which anxiety symptoms are prominent which comprises administering a non-toxic anxiolytically effective dose of buspirone or a pharmaceutically acceptable acid addition salt thereof to a neurotic patient." (Claim 1.)

The dependent claims define, inter alia, route of administration and daily dose quantities.

8. The named inventors continued to believe that they were the only joint inventors of the invention of the '763 patent until the time that they were shown a document that was prepared by Dr. John E. Gajewski. [Attached hereto as Exhibit A.] The document was dated April 23, 1974, which was prior to the time that the named inventors made the invention beginning in about mid-1975.

9. Each named inventor individually states with respect to himself:

(a) That he saw Exhibit A for the first time between about late 1984 and about September 1985;

(b) That he did not know of the existence of Exhibit A prior to the first time that he saw it;

(c) That he did not know that Dr. Gajewski had prepared Exhibit A prior to the first time that he saw it;

(d) That he was shown Exhibit A for the first time by patent attorneys for the assignee of the '763 patent;

(e) That he was advised by said attorneys of the meaning within the context of the U.S. patent laws of "inventorship," and he was advised of the requirement for naming all inventors on a U.S. patent application and patent; and

(f) That he, after reading and understanding Exhibit A, and accepting the advice of said attorneys, now believes that Dr. Gajewski is a joint inventor of the invention disclosed and claimed in the '763 patent.

10. The named inventors, individually and jointly, now realize and believe that an error was made in failing to include Dr. Gajewski as an applicant and joint inventor on S.N. 908,597 and as a joint inventor on the '763 patent, together with the named inventors.

11. The named inventors, individually and jointly, believe that the error in not including Dr. Gajewski on S.N. 908,597 occurred because of their lack of knowledge of the existence of Exhibit A. The named inventors believe that the reason that none of them saw or knew about Exhibit A prior to the time it was shown to each of them, as set forth in Paragraph 9, above, is that none of them were in the chain of

responsibility at Mead Johnson and Bristol-Myers that would have been the basis for any of them receiving a copy of Exhibit A and/or being advised of its existence.

12. The named inventors, individually and jointly, understand that Exhibit A describes the method of at least claim 1 of the '763 patent, particularly by suggesting the usefulness of buspirone as an antianxiety agent in neurotic patients.

13. The named inventors believe that the application that was filed as S.N. 908,597 was prepared by Dr. Robert E. Carnahan, a patent agent employed by the Bristol-Myers Company. To the best of their recollection, individually and jointly, Dr. Carnahan reviewed those internal documents of Mead Johnson that were dated contemporaneously with the making of the joint invention by the named inventors (i.e., about mid-1975), and later, and in discussions with the named inventors, they jointly and individually expressed to Dr. Carnahan their then held belief that the named inventors were the only joint inventors. They also believe, that at the time Dr. Carnahan prepared the application, Dr. Carnahan, based on such information as described above, believed that the named inventors were the only joint inventors, and he prepared and sent to the named inventors the declaration for the named inventors. The named inventors signed the declaration in the belief that they were the only joint inventors.

14. In view of the facts as set forth above, and the explanations made to the named inventors by said attorneys

with respect to the meaning of the term "inventorship," the named inventors, individually and jointly, believe that Dr. Gajewski is a joint inventor together with the named inventors for the subject matter described and claimed in the '763 patent, and that Dr. Gajewski was omitted as a joint inventor together with the named inventors through error. The named inventors believe, individually and jointly, that such error occurred without any deceptive intention by any of the named inventors, or Dr. Gajewksi, or anyone else involved with the preparation and prosecution of S.N. 908,597 or anyone else in privy with any of these people, and the named inventors have no reason to believe that the error occurred with deceptive intention.

15. The named inventors are informed and believe, individually and jointly:

(a) That the error without deceptive intention was discovered by one of the attorneys who first showed the named inventors Exhibit A;

(b) That the attorney had come across document Exhibit A during the course of his review of older Mead Johnson documents (i.e., dated prior to about mid-1975) bearing on busipirone as an antipsychotic agent in connection with his assigned task of reviewing the '763 patent, including the history of the making of the invention claimed in the '763 patent;

(c) That the review by the attorney was commenced in about late 1984 at which time he began to gather information in aid of his review of the '763 patent;

(d) That Exhibit A was discovered by the attorney in the course of gathering the information in about late 1984;

(e) That the attorney continued his investigation and review of the '763 patent for several more months prior to preparing his report in about April 1985;

(f) That the attorney together with other attorneys of Bristol-Myers thereafter undertook further legal and factual (including further interviews) analyses and considerations on the question of whether Dr. Gajewski was a joint inventor;

(g) That it was not until about August 1985 that the decision was made to petition the Commissioner of Patents and Trademarks for a Certificate of Correction to add the name of Dr. Gajewski as an inventor on the '763 patent; and

(h) That it took about two months to complete the necessary interviews and the necessary papers that were required to prepare the petition for the Certificate of Correction to correct the inventorship of the '763 patent.

16. In view of the facts as set forth above, the named inventors, individually and jointly, believe that it was in about mid-1985 that the error was discovered to exist in fact.

17. Accordingly, the named inventors petition the Commissioner of Patents and Trademarks to correct the inventorship error and issue a Certificate of Correction that adds the name of John E. Gajewski as an inventor on the '763 patent.

We, the named inventors hereby declare, individually and jointly, that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the '763 patent.

Dated: 9-26-85 George P. Casten
George P. Casten

Dated: Sept. 27, 1985 Gordon R. McKinney
Gordon R. McKinney

Dated: September 25, 1985 Roger E. Newton
Roger E. Newton

Dated: September 30, 1985 E. Crosby Tompkins
E. Crosby Tompkins

Dated: September 26, 1985 John H. Weikel, Jr.
John H. Weikel, Jr.

BRISTOL-MYERS COMPANY
PHARMACEUTICAL, HEALTH CARE, AND INTERNATIONAL GROUP
R & D PROJECT EVALUATION
I - NARRATIVE SUMMARY

PROJECT/~~PROGRAM~~ (6)	B-M DIVISION
Buspirone - Project 9022	Mead Johnson and Company for BMCID
PATENT STATUS	LICENSOR
PREPARED BY: DATE:	APPROVED BY: DATE:
J. E. Gajewski April 23, 1974	W. M. Govier 5/15/74

PRODUCT DESCRIPTION, CHARACTERISTICS AND RISKS

To further delineate the neuropharmacologic spectrum especially its usefulness as an anti-anxiety agent in psychotic and neurotic patients alone and in comparison with presently used anxiolytic agents.

SUMMARY OF ANTICIPATED CHALLENGES AND OPPORTUNITIES

Safety and tolerance studies in normal subjects demonstrated that the margin of safety was much higher than predicted from laboratory models. Acute psychotic patients (schizophrenics) showed a tolerance many times greater than normal subjects. Although as a neuroleptic agent, the quantitative response in comparison to presently used agents was low, analysis of the rating scales revealed that relief of anxiety in acute psychotic patients was highly significant, suggesting that perhaps it might be a useful anxiolytic in neurotic patients. Since there are several widely used very efficacious anxiolytic agents available, the costs involved in evaluating this compound as an anxiolytic may not be justified in relationship to the anticipated return if it were marketed.

Probability of Success: 20%

EXHIBIT A

WHAT IS CLAIMED IS:

1. A method for the palliative treatment of neurosis in which anxiety symptoms are prominent which comprises administering a non-toxic anxiolytically effective dose of buspirone or a pharmaceutically acceptable acid addition salt thereof to a neurotic patient.

2. The method of Claim 1 wherein buspirone hydrochloride is employed, and dosage is by the oral route.

3. The method of Claim 2 wherein said patient is suffering from anxiety neurosis.

4. The method of Claim 2 wherein said patient is suffering from anxiety neurosis with depressive symptoms.

5. The method of Claims 2, 3, or 4 wherein said patient is an adult and a daily dose of from 20 mg. to 60 mg. is employed.

6. The method of Claim 5 wherein said daily dose is divided and administered b.i.d.

7. The method of Claim 5 wherein said daily dose is divided and administered t.i.d.

8. The method of Claim 2 wherein the maximum total daily dose of up to about 100 mg.

9. The method of Claims 2, 3, or 4 wherein said patient is an adult and a daily dose of from 20 mg. to 30 mg. is employed.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.:	4,182,763
Named Inventors:	George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins and John H. Weikel, Jr.
For:	BUSPIRONE ANTI-ANXIETY METHOD
Issued:	January 8, 1980
Serial No.:	908,597
Filed:	May 22, 1978
Group Art Unit:	125
Examiner:	Stanley J. Friedman

Duplicate

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

DECLARATION, POWER OF ATTORNEY AND PETITION
UNDER 37 C.F.R. §1.63
FOR APPLICATION S.N. 908,597 NOW
U.S. PATENT NO. 4,182,763

We, GEORGE P. CASTEN, GORDON R. McKINNEY, ROGER E. NEWTON, E. CROSBY TOMPKINS, JOHN H. WEIKEL, JR. and JOHN E. GAJEWSKI declare as follows:

1. I, GEORGE P. CASTEN, declare that I am a citizen of the United States of America residing at 7416 Adams Avenue, Evansville, Indiana 47715.

2. I, GORDON R. McKINNEY, declare that I am a citizen of the United States of America residing at 421 Kings Valley Road, Evansville, Indiana 47711.

3. I, ROGER E. NEWTON, declare that I am a citizen of the United States of America residing at 1400 Lark Drive, Evansville, Indiana 47715.

4. I, E. CROSBY TOMPKINS, declare that I am a citizen of the United States of America residing at 15119 Fairmont Court, Grand Haven, Michigan 49417.

5. I, JOHN R. WEIKEL, JR., declare that I am a citizen of the United States of America residing at R.R. #4, Box 266, Mount Vernon, Indiana 47620.

6. I, JOHN E. GAJEWSKI, declare that I am a citizen of the United States of America residing at 767 South Hebron Avenue, Evansville, Indiana 47715.

7. We each verily believe that we are the original, first and joint inventors of the invention entitled "Buspirone Anti-Anxiety Method," described and claimed in the specification filed May 22, 1978 as Application Serial No. 908,597 that was issued as U.S. Patent No. 4,182,763 on January 8, 1980; that we each reviewed and understand the contents of said application and patent; that, as to the subject matter of this application and patent, we each do not know and do not believe that this invention was ever known or used in the United States of America before our invention thereof, or patented or made the subject of an inventor's certificate or described in any printed publication in any country before our invention thereof, or more than one year prior to May 22, 1978; or in public use or on sale in the United States of America more than one year prior to May 22, 1978; that the said subject matter has not been patented or made the subject of an inventor's certificate before May 22, 1978 in any country foreign to the United States on an application filed by us or our legal representatives or

assigns more than twelve months before May 22, 1978; that we each acknowledge our duty to disclose information of which we each are aware which is material to the examination of this application; and that no application for patent or an inventor's certificate on said subject matter has been filed by us or our representatives or assigns in any country foreign to the United States of America prior to May 22, 1978.

8. We hereby appoint Robert E. Carnahan, Registration No. 18,500, Bristol Laboratories, Bristol-Myers Company, P.O. Box 4755, Syracuse, New York 13221-4755, Telephone No. (315) 432-4813, our agent with full power of substitution and revocation, to prosecute the petition for Certificate of Correction and to transact all business in the Patent and Trademark Office connected therewith. Please address all communications to Dr. Carnahan.

9. Wherefore we pray that said U.S. Patent No. 4,182,763 be corrected to add the name of John E. Gajewski as an inventor of said U.S. Patent No. 4,182,763.

10. We make this Declaration, Power of Attorney and Petition under 37 C.F.R. §1.63 For Application S.N. 908,597 now U.S. Patent No. 4,182,763 in support of the Petition Under 37 C.F.R. §1.324 to correct inventorship by adding the name of John E. Gajewski as an inventor on U.S. Patent No. 4,182,763, and we hereby subscribe our names to this Declaration, Power of Attorney and Petition under 37 C.F.R. §1.63 For Application S.N. 908,597 now U.S. Patent No. 4,182,763.

We, the undersigned, declare further that all statements herein of our own knowledge are true and that all

statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of U.S. Patent No. 4,182,763.

Inventor's Name and Signature: George P. Casten
George P. Casten

Date: 9-26-85

Post Office Address: 7416 Adams Avenue
Evansville, Indiana 47715

Inventor's Name and Signature: Gordon R. McKinney
Gordon R. McKinney

Date: Sept. 27, 1985

Post Office Address: 421 Kings Valley Road
Evansville, Indiana 47711

Inventor's Name and Signature: Roger E. Newton
Roger E. Newton

Date: September 25, 1985

Post Office Address: 1400 Lark Drive
Evansville, Indiana 47715

Inventor's Name and Signature: E. Crosby Tompkins
E. Crosby Tompkins

Date: September 30, 1985

Post Office Address: 15119 Fairmont Court
Grand Haven, Michigan 49417

Inventor's Name and Signature: John N. Weikel, Jr.
John N. Weikel, Jr.

Date: Sept. 26, 1985

Post Office Address: R.R. #4, Box 266
Mount Vernon, Indiana 47620

Inventor's Name and Signature: John E. Gajewski
John E. Gajewski

Date: 27 Sept 1985

Post Office Address: 767 South Hebron Avenue
Evansville, Indiana 4771

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No. 4,182,763
Grant Date: January 8, 1980
Patentees: George P. Casten, et al.
Title: Buspirone Anti-Anxiety Method

Honorable Commissioner of Patents
and Trademarks
Washington, D. C. 20231

LETTER

The undersigned, principal agent identified in the file of this patent, submitted a Petition for Certificate of Correction under 37CFR1.322 Office Mistake on October 4, 1985. That petition has not yet been acted upon and in fact has been placed in the patented file. It is believed that this is an oversight on the part of the Office which occurred in the course of considering another Petition for Certificate of Correction filed at the same time. The latter involved a change of inventorship and was issued on March 18, 1985.

Prompt remedy of the above oversight is requested. Bristol-Myers Company, assignee of the above patent, has invested substantial sums of money in development of the claimed invention over the last ten years, and has reason to believe that marketing approval by the Federal Food and Drug Administration will be received soon. An application for extension of the term of the patent under 35 USC 156 has been prepared and will be filed promptly following approval the New Drug Application. Copies of Certificates of Correction must be included in such application in accordance with Guidelines Section D(b)(7), and accordingly it is imperative that action on the pending Petition be

PRINTER'S TRIM LINE

Staple here Only

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 4,182,763

DATED : January 8, 1980

INVENTOR(S) : George P. Casten et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 8, line 5, Claim 5, delete "2, 3 or 5" and insert -- 2, 3 or 4 --.

Staple Here Only !

PRINTER'S TRIM LINE

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 4,182,763

DATED : January 8, 1980

INVENTOR(S) : (As Named) George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins, John H. Weikel, Jr.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the title page, in line designated "[75] Inventors", after "John H. Weikel, Jr., Mt. Vernon," insert --John E. Gajewski, Evansville,--.

Staple Here Only 1

PRINTER'S TRIM LINE

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 4,182,763

DATED : January 8, 1980

INVENTOR(S) : (As Named) George P. Casten, Gordon R. McKinney, Roger E. Newton, E. Crosby Tompkins, John H. Weikel, Jr.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Col. 8, line 5, (in claim 5) delete

"2, 3 or 5" and insert therefore

--2, 3 or 4--.

United States Patent [19]

Casten et al.

[11] 4,182,763

[45] Jan. 8, 1980

[54] **BUSPIRONE ANTI-ANXIETY METHOD**

[75] Inventors: George P. Casten; Gordon R. McKinney; Roger E. Newton; E. Crosby Tompkins, all of Evansville; John H. Weikel, Jr., Mt. Vernon, all of Ind.

[73] Assignee: Mead Johnson & Company, Evansville, Ind.

[21] Appl. No.: 908,597

[22] Filed: May 22, 1978

[51] Int. Cl.[2] A61K 31/505

[52] U.S. Cl. 424/251

[58] Field of Search 424/251

[56] References Cited

U.S. PATENT DOCUMENTS

3,717,634 2/1973 Wu et al. ..... 260/256.4 N

3,976,776 8/1976 Wu et al. 424/251

OTHER PUBLICATIONS

Wu et al., J. Med. Chem. 15, (1972), pp. 477–479.

Allen et al., Arzneim-Forsch, 24, No. 6, 917–992 (1974).

Sathancenthan et al., Current Therapeutic Research, 18, (5), 701–705 (1975).

Primary Examiner—Stanley J. Friedman

Attorney, Agent, or Firm—R. E. Carnahan; R. H. Uloth

[57] ABSTRACT

Buspirone hydrochloride is an effective anti-anxiety agent for the palliative treatment of neurotic patients in which symptoms of anxiety are predominant at doses which are without observable effect in either normal individuals or psychotic patients.

9 Claims, No Drawings

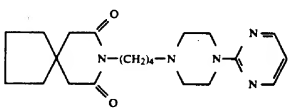
BUSPIRONE ANTI-ANXIETY METHOD

FIELD OF THE INVENTION

This invention is concerned with a drug bio-affecting and body-treating process which employs the pyrimidine compound 8-[4-[4-(2-pyrimidinyl)-1-piperazinyl]-butyl]-8-azaspiro[4.5]decane-7,9-dione or a pharmaceutically acceptable acid addition salt thereof (Class 424, Subclass 251).

DESCRIPTION OF THE PRIOR ART

The pyrimidine compound with which the present invention is concerned has the following structural formula



The hydrochloride salt has been referred to in the prior art as MJ 9022-1 and as buspirone hydrochloride. Other acid addition salts thereof are named by combining "buspirone" with the appropriate word to define the acid from which it is prepared as in "buspirone hydrochloride." The latter is the United States Adopted Name (USAN). Refer to J. Amer. Med. Assoc. 225, 520 (1973).

The synthesis of the compound and the identification of its psychotropic properties typical of the major tranzuilizers such as chlorpramazine are described in the following patents and publications.

1. Y. H. Wu, et al., J. Med. Chem. 15, 477 (1972) "Psychosedative Agents. 2. 8-(4-Substituted 1-Piperazinylalkyl)-8-azaspiro[4.5]decane-7,9-diones".

2. Y. H. Wu, et al., U.S. Pat. No. 3,717,634 patented Feb. 20, 1973. "N-(Heteroarcyclic)piperazinylalkylazaspiroalkanediones".

3. L. E. Allen, et al., Arzneim.-Forsch. 24, Nr. 6, 917-922 (1974). "Pharmacologic Effects of MJ 9022-1, a Potential Tranquilizing Agent."

4. G. L. Sathananthan, et al., Current Therapeutic Research, 18, (5), 701-705 (1975). "MJ 9022: Correlation Between Neuroleptic Potential and Stereotypy."

5. Y. H. Wu, et al., U.S. Pat. No. 3,976,776 patented Aug. 24, 1976. "Tranquilizer Process Employing N-(Heteroarcyclic)piperazinylalkylazaspiroalkanediones."

SUMMARY OF THE INVENTION

The process of the present invention is intended for the palliative treatment of neurosis with buspirone or a pharmaceutically acceptable acid addition salt thereof where anxiety symptoms are prominent. Pharmaceutically acceptable acid addition salts of buspirone and methods of pharmaceutical formulation are described in the above patent (2) of Y. H. Wu, et al., U.S. Pat. No. 3,717,634 which is incorporated herein in its entirety by reference. The process is specifically intended for adult patients who present with manifest anxiety characterized by an affective state which may occur under many clinical circumstances and in diverse pathologic contexts. It is also applicable to children in similar circumstances.

Neurosis is a functional nervous disorder without demonstrable physical lesion. Neuroses are defined in "Diagnostic and Statistical Manual of Mental Disorders" 2nd Edition, published by American Psychiatric Association, 1968 (Library of Congress Catalog No. 6826515) as follows (page 39).

"Anxiety is the chief characteristic of the neuroses. It may be felt and expressed directly, or it may be controlled unconsciously and automatically by conversion, displacement and various other psychological mechanisms. Generally, these mechanisms produce symptoms experienced as subjective distress from which the patient desires relief.

"The neuroses, as contrasted to the psychoses, manifest neither gross distortion or misinterpretation of external reality, nor gross personality disorganization. A possible exception to this is hysterical neurosis, which some believe may occasionally be accompanied by hallucinations and other symptoms encountered in psychoses.

"Traditionally, neurotic patients, however severely handicapped by their symptoms, are not classified as psychotic because they are aware that their mental functioning is disturbed."

Anxiety neurosis is defined in the same reference as follows (page 39).

"This neurosis is characterized by anxious over-concern extending to panic and frequently associated with somatic symptoms. Unlike Phobic neurosis (q.v.), anxiety may occur under any circumstances and is not restricted to specific situations or objects. This disorder must be distinguished from normal apprehension or fear, which occurs in realistically dangerous situations."

The present process is concerned with the treatment of anxiety neuroses, and is to be distinguished from prior psychotherapeutic processes employing buspirone which dealt with psychoses. The following definition of psychoses is quoted from the above cited "Diagnostic and Statistical Manual of Mental Disorders" for the purpose of differentiating "psychoses" from "neuroses."

"Patients are described as psychotic when their mental functioning is sufficiently impaired to interfere grossly with their capacity to meet the ordinary demands of life. The impairment may result from a serious distortion in their capacity to recognize reality. Hallucinations and delusions, for example, may distort their perceptions. Alterations of mood may be so profound that the patient's capacity to respond appropriately is grossly impaired. Deficits in perception, language and memory may be so severe that the patient's capacity for mental grasp of his situation is effectively lost."

Different classes of drugs have been used in the past for the treatment of neuroses and psychoses and no relationship has developed among the drugs which are applicable to the treatment of these two distinct conditions. The psychoses are mainly treated with the phenothiazines with chloropromazine being representative of this class. The anti-anxiety agents or anxiolytics are drawn from a number of structural classes but the benzodiazopines, with diazepam as a specific example, include the majority of drugs used for this purpose. Buspirone is structurally unrelated to any other drug used in the treatment of neuroses.

Administration of buspirone according to the present invention may be by the parenteral, oral, or rectal

routes. The oral route is, however, preferred and there is, in fact, little need to employ other means of administration such as subcutaneous, intramuscular, or intravenous injection. The reason for this is that neurotic patients for whom the process is applicable are rational individuals, are generally treated on an out-patient basis, and are able to cooperate with the physician or psychiatrist. Generally speaking, the effectiveness of the method soon becomes evident to the patient and ensures his cooperation.

Dosage amounts are less than about 100 mg. per day and preferably in the range of 20–30 mg. per day. In exceptional cases, it may be necessary to increase the dose to about 60 mg. per day. Since the dosage must be tailored to the individual patient, the usual practice is to commence with a dose of 5 mg. administered two or three times per day and to then increase the dose every two or three days by 5 mg. at each dosage time until the desired response is observed or until the patient complains of side effects. Single daily dosage is applicable in some instances. The duration of treatment is extended until the patient's symptoms have substantially disappeared and a symptom-free period has elapsed. Usual periods of treatment are from one to three months. Treatment may be re-instituted at any time that symptoms reappear.

The dosage range referred to above serves to emphasize the distinction between the present process and the treatment of psychotic patients with buspirone as has been described in the prior art (G. L. Sathananthan, et al. op cit.) in which doses of from 600 to 2400 mg. per day of buspirone hydrochloride were required to demonstrate neuroleptic action in psychotic patients. The dosage range of 10 to 100 mg. per day which is applicable to neurotic patients to achieve an anxiolytic effect is without adverse effect in a normal individual and without neuroleptic effect in a psychotic patient for whom treatment with an anti-psychotic agent or major tranquilizer is indicated.

DETAILED DESCRIPTION OF THE INVENTION

The patients for treatment according to the present invention are minimally characterized by the first two manifestations listed below which are exhibited to a modrate or high degree of severity and preferably at least three of the others listed as (3) through (17).

Subjective Experiences:

(1) Feeling nervous, jittery, jumpy
(2) Feeling fearful, apprehensive, anxious, panicky
(3) Fears of fainting, screaming, losing control, crowds, places, disaster, death
(4) Avoiding certian places, things, or activities because of fear
(5) Feeling tense or keyed up

Muscular or Motor Phenomena:

(6) Tense, aching muscles
(7) Trembling, shaking
(8) Restlessness, fidgeting

Autonomic Phenomena:

(9) Heart beating fast or pounding; chest pain
(10) Trouble catching breath, air hunger, smothering, lump in throat, choking
(11) Sweating, especially armpits, palms, soles of feet
(12) Cold, clammy hands
(13) Dry mouth
(14) Dizziness, faintness, lightheadedness, weakness
(15) Tingling feelings in hands or feet
(16) Stomach "gas", nausea, upset stomach
(17) Frequency or urgency of bladder or bowels

The patients are preferably rated before commencing treatment according to one or more of the established psychometric rating scales for neurotic patients. The same psychometric methods may then be used to evaluate the patient periodically during the treatment period, preferably every 2 or 3 days until the appropriate dosage schedule has been determined and then at weekly intervals.

Various suitable rating scales have been described in the literature. They have been collected in a form readily adapted to clinical use by the U.S. Department of Health, Education and Welfare in a volume by William Guy entitled "ECDEU Assessment Mannual for Psychopharmacology," Revised 1976, National Institute of Mental Health, 5600 Fishers Lane, Rockville, Maryland 20852 (DHEW Publication No. (ADM)76-338). ECDEU is an acronym for Early Clinical Drug Evaluation Unit. Some of these psychometric rating scales which are suitable for this invention are listed below. The page numbers refer to the foregoing collection.

Hamilton Anxiety Scale	page 193
Hamilton Depression Scale	page 179
Self Report Symptom Inventory	page 313
Profile of Mood States	page 529
Hopkins Symptom Checklist	page 575
Self Rating Symptom Scale	page 579
Clinical Global Impressions	page 217

Other Rating scales as may suit the psysician or psychiatrist may also be employed. Also, other tests as may be deemed desirable by the physician or psychiatrist in accord with good medical practice should be employed such as a complete medical history and physical examination.

Dosage is commenced at from 10 mg. to 20 mg. per day, and then increased step-wise until an anxiolytically effective dose is achieved without toxic effect. The dose may then be reduced to establish the optimal effect-minimal dose relationship. This usually occurs in the range of 20–30 mg. per day, but doses as high as 60 mg. per day may be employed. Doses as high as about 100 mg. are without substantial adverse effects in normal or neurotic individuals. Dosage on a b.i.d. or t.i.d. schedule is preferred.

DESCRIPTION OF SPECIFIC EMBODIMENTS

EXAMPLE 1

Open Study.—Thirty patients diagnosed as suffering from anxiety reaction were entered into an evaluation of buspirone hydrochloride for treatment of the condition. Seven of the thirty patients also exhibited significant symptoms of depression in addition to their predominating symptoms of anxiety reaction. The duration of the study was four weeks. Seven patients dropped out of the study and were not included in the analysis of the results. Two of these suffered side effects by the second day of treatment, one was improved by the seventh day of treatment, and the other four were lost to follow-up for unknown reasons. All patients entered into the study had a rating on the Hamilton Anxiety Scale (op. cit.) of at least 18 on entry into the study. Anxiety symptoms had been present for at least a month in all cases, and 19 had suffered the symptoms for a year or more. None of the patients exhibited evidence of

schizophrenia, affective psychosis, convulsive disorders, organic brain syndrome, strong sociopathy, drug addiction, or alcoholism. The patients were rated on entry into and at the conclusion of the study and weekly according to the Hamilton Anxiety Scale (HAM-A op. cit.), the Hamilton Depression Scale (HAM-D op. cit.), and by a physician's questionaire (PQ) according to which severity of the disease was rated on the following scale: 1—not ill; 2—very mild; 3—mild; 4—moderate; 5 moderately severe; 6—severe; 7—extremely severe. Other rating methods were also used. The following table shows the average daily dose, and the rating scale results. The HAM-A and HAM-D ratings at the end of the study were within the normal range, and the PQ rating indicated only very mild remaining anxiety.

AVERAGE ANXIETY RATINGS AND DOSAGES

	Daily Dose (mg.)	HAM-A	HAM-D	PQ	n[3]
Outset	0	21.5	12.1	4.5	23
Week 1	21.3	11.0[1]	8.8[2]	3.6[2]	23
Week 2	25.1	8.3[1]	7.4[2]	2.9[2]	16
Week 3	24.1	5.5[1]	4.8[1]	2.5[2]	13
Week 4	19.9	2.8[1]	3.7[1]	2.3[2]	12

[1]Paired t-test relative to outset values significant @ 0.01 level.
[2]Paired t-test relative to outset values significant @ 0.05 level.
[3]Number of patients included in evaluation.

EXAMPLE 2

Double Blind Study.—Sixty adult out-patients with manifest anxiety were selected for a double-blind parallel study. Twenty patients were entered into each of three groups. One group was treated with buspirone hydrochloride, 5 mg. capsule, another with diazepam, 5 mg. tablet contained within a matching capsule, and the third with placebo, inert ingredients in a matching capsule. The starting dose was one capsule b.i.d. (buspirone hydrochloride 10 mg. or diazepam 10 mg.) and the dose was increased by one or two capsules every two or three days depending upon therapeutic response and side effects. The maximum dose allowable was 60 mg. per day of buspirone hydrochloride or diazepam. Laboratory and physical examinations were conducted on admission and at termination of the study and a number of standard psychometric rating scales were administered on admission, at weekly intervals, and at termination of the study. The study duration was four weeks. The results based upon the degree of improvement in the physician's evaluation and in the patient's own evaluation are given in the following table. The status of the patients at the end of the study is given, as well as the cumulative results which include drop-outs evaluated at an interim period.

PHYSICIAN AND PATIENT EVALUATION OF THERAPEUTIC EFFECT

Treatment At:	No. Patients In Study	No. Patients Dropout	Therapeutic Effect at Termination (No. Patients) Physician Evaluation Marked	Moderate	Minimal	Patient Evaluation Much	Moderately	A Little	Average Daily Dose (mg.)
END OF STUDY									
Buspirone	14	6[1]	8	4	2	10	1	3	23.7[5]
Diazepam	14	6[2]	7	4	3	9	2	3	26.4[5]
Placebo	10	10[3]	1	2	7	3	—	7	
CUMULATIVE RESULTS:									
Buspirone	18	2[4]	10	4	3	12	3	3	19.6
Diazepam	20	none	7	6	7	10	3	7	18.7
Placebo	18	2[4]	1	2	15	3	—	15	

[1]One dropped out because of side effects; one due to unrelated illness; two because of improvement; two for unknown reasons.
[2]Three dropped out because of side effects, one due to unrelated changed life situation, two because of improvement.
[3]Two dropped out during the first week for unknown reasons, the remainder dropped out subsequently due to lack of improvement.
[4]Drop-outs where no interim evaluation was obtained.
[5]During fourth week.

The therapeutic effect with buspirone hydrochloride was comparable to that obtained with diazepam. Buspirone had fewer side effects than either diazepam or placebo. Only three patients complained of side effects under buspirone. These occurred within the first two weeks and only one patient dropped out because of side effects (moderate dizziness, cold sweat). Ten patients complained of side effects under diazepam but only three dropped out for this reason (weakness, tiredness, nausea, vomiting, insomnia, vivid dreams, drowziness, depression, dry mouth, dizziness, excitement, confusion, tachycardia, tremor, blurred vision, and headache). Six patients complained of side effects under placebo but none dropped out for this reason. Placebo drop-outs were due to lack of therapeutic effect. In addition, buspirone appeared to be effective in relieving depression in patients presenting with mixed anxiety and depression symptoms. Sleep information gathered during the study indicated that the patients slept more deeply under diazepam in contrast to the lighter sleep reported by the buspirone patients. A deeper sleep would accord with the sedation action of diazepam.

EXAMPLE 3

Buspirone Hydrochloride 5 mg. and 10 mg. Tablets.-The following ingredients are employed.

	5 mg. Tablet	10 mg. Tablet
Buspirone Hydrochloride	5.0 mg	10.0 mg
Lactose, Anhydrous Direct compression	55.7	111.4
Starch, Sodium Carboxy-Methyl	8.0	16.0
Cellulose, Microcrystalline, NF	30.0	60.0
Colloidal Silicon Dioxide	0.5	1.0
Magnesium Stearate	0.8	1.6
TOTAL	100.0	200.0

Processing Instructions:
1.0 Blend in a suitable mixer:
(a) Colloidal Silicon Dioxide
(b) Cellulose, Microcrystalline, NF
2.0 Pass the blended material from Step 1 through a screen.
3.0 Blend in a suitable mixer:
(a) Screened powder from Step 2

(b) Buspirone Hydrochloride
(c) Lactose, Anhydrous DC
(d) Starch, Sodium Carboxy-Methyl
(e) Cellulose, Microcrystalline, NF
(f) Magnesium Stearate

4.0 Compress the granulation into tablets.

What is claimed is:

1. A method for the palliative treatment of neurosis in which anxiety symptoms are prominent which comprises administering a non-toxic anxiolytically effective dose of buspirone or a pharmaceutically acceptable acid addition salt thereof to a neurotic patient.

2. The method of claim 1 wherein buspirone hydrochloride is employed, and dosage is by the oral route.

3. The method of claim 2 wherein said patient is suffering from anxiety neurosis.

4. The method of claim 2 wherein said patient is suffering from anxiety neurosis with depressive symptoms.

5. The method of claims 2, 3, or 5 wherein said patient is an adult and a daily dose of from 10 mg. to 60 mg. is employed.

6. The method of claim 5 wherein said daily dose is divided and administered b.i.d.

7. The method of claim 5 wherein said daily dose is divided and administered t.i.d.

8. The method of claim 2 wherein the maximum total daily dose of up to about 100 mg.

9. The method of claims 2, 3, or 4 wherein said patient is an adult and a daily dose of from 20 mg. to 30 mg. is employed.

* * * * *